



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|------------------------------|------------------|
| 10/824,593 | 04/15/2004 | Raymond Pratt | 109536.159WO1 | 6645 |
| 26694 | 7590 | 05/10/2007 | EXAMINER | |
| VENABLE LLP P.O. BOX 34385 WASHINGTON, DC 20043-9998 | | | CHANNAVAJALA, LAKSHMI SARADA | |
| ART UNIT | | PAPER NUMBER | | |
| 1615 | | | | |
| MAIL DATE | | DELIVERY MODE | | |
| 05/10/2007 | | PAPER | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | |
|------------------------------|--------------------------|--------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 10/824,593 | PRATT ET AL. |
| | Examiner | Art Unit |
| | Lakshmi S. Channavajjala | 1615 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 11 April 2007.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 25-45 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 25-45 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt of response dated 4-11-07 is acknowledged.

Claims 25-45 are pending in the instant application.

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn. Upon careful review, the following new rejection has been applied to the instant claims:

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/39000 (WO) in view of US 5,278,176 to Lin or WO in view of Buccafusco et al (Brain Research). Applicants have cited WO and Buccafusco on PTO-1449, however, a full article of Buccafusco have been attached to this action.

WO teaches methods of treating disorders of attention or improving attention by administering an effective amount of a cholinesterase inhibitor. WO teaches that acetylcholine is a neural transmitter for transmitting messages across the synapse to a cholinergic message by stimulating the cholinergic receptor for neuronal messages such as memory (page 3, L 23-29). WO teaches that cholinesterase rapidly destroys acetylcholine resulting in a weak cholinergic stimulation, experienced as a memory loss, and states that one way to overcome the above loss is to interfere with the ability of cholinesterase to degrade acetylcholine, as by treatment with a cholinesterase inhibitors

(page 4, l 5-12). WO teaches all of the instant claimed compounds, including donepezil, for their cholinesterase inhibiting activity and thus inhibiting memory loss (pages 5+). WO fails to teach the claimed method of treating substance abuse or treating withdrawal symptoms or decreasing the rate of relapse.

Lin teaches selective and potent nicotinic agonists that are useful in treating dementias, attention disorders, and anxiety associated with cognitive impairment or substance abuse withdrawal characterized by decreased cholinergic function (abstract). Lin teaches that chronic alcoholism (reads on instant substance abuse, see instant claim 36) and the resultant brain disease such as Alzheimer's disease, is characterized by diffuse reductions in cortical cerebral blood flow in those brain regions where cholinergic neurons arise (col. 2, L 61-65). Lin further states that nicotine withdrawal syndrome associated with tobacco use is characterized by craving for nicotine, irritability, frustration, anger, difficulty in concentration etc (col. 4, L 60-67). Lin suggests that symptoms associated with withdrawal of nicotine or compounds that act as nicotine agonists for acetylcholine receptors can alleviate other addictive substances.

Buccafusco et al studied the prevention of precipitated withdrawal symptoms by activating cholinergic systems during a dependence-producing schedule of morphine in rats. Buccafusco teaches that central cholinergic neurons have long been suggested to mediate many of the signs and symptoms of opiate withdrawal, profoundly affected by morphine and related drugs (page 76, col. 2 through page 77, col.1). Buccafusco observed that the many of the withdrawal symptoms such as body shakes were

significantly reduced by treatment with cholinergic drugs (page 81, section 3.41).

Buccafusco also observed that the AchE (acetylcholine esterase) activity was reduced upon administration of DFP (diisopropylfluorophosphate), a cholinesterase inhibitor.

Buccafusco further observed a significant reduction in each of the spontaneous morphine induced withdrawal symptoms, post-withdrawal blood pressure and the accompanying loss in body weight (page 81).

Thus, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use the cholinesterase inhibitors such as donepezil and other compounds of treating substance abuse or withdrawal symptoms associated with substance abuse because both Lin and Buccafusco emphasize that the cholinergic system plays a profound role in substance abuse or drug withdrawal symptoms that are associated with substances such as alcohol or morphine (both of which are claimed to cause substance abuse) and that cholinesterase inhibitors effectively interfere with and alleviate the substance abuse and the associated withdrawal symptoms. Thus, on of an ordinary skill in the art would have expected the cholinesterase inhibitors of WO to be effective in reducing the substance abuse or in interfering with the drug withdrawal symptoms caused by abusive drugs such as nicotine, morphine, alcohol etc.

While Lin or Buccafusco does not teach all of the claimed drugs that result in the abuse or cause the withdrawal symptoms, both of them teach the underlying mechanism that results in the claimed abuse and its withdrawal symptoms and hence a skilled artisan would have expected to effectively reduce substance abuse, caused by any substance, with the cholinesterase inhibitors of WO. Further, optimizing the amount

Art Unit: 1615

and the route of administration of the compounds of WO, so as to reduce substance addiction and also prevent the return to drug seeking behavior would have been within the scope of a skilled artisan.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.00 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AU 1615

5/1/05


LAKSHMI S. CHANNAVAJJALA
PRIMARY EXAMINER

Application/Control Number: 10/824,593
Art Unit: 1615

Page 6

May 7, 2007